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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/816,591 | 04/01/2004 | Laura Fuertes-Lopez | FUERTES-LOPEZ | 8510 |

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| EXAMINER | |
|---|---|
| WEHBE, ANNE MARIE SABRINA | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1633 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/816,591 | FUERTES-LOPEZ ET AL. | |
| | Examiner | Art Unit | |
| | Anne Marie S. Wehbe | 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *5/9/08*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicant's amendment and response received on 5/9/08 has been entered. Claims 1-23 are canceled. Claim 24 as been amended and is currently pending and under examination in the instant application.

Those sections of Title 35, US code, not included in this action can be found in the previous office action.

### *Priority*

Applicant's claim for foreign priority based on applications filed in Germany on October 2, 2001 or November 12, 2001, is acknowledged. It is further acknowledged that certified copies in German for both priority documents, DE 101 56 679.4, and DE 101 48 732.0 as required by 35 U.S.C. 119(b) are now of record in this application.

### *Claim Rejections - 35 USC § 103*

The rejection of claim 24 under 35 U.S.C. 103(a) as being unpatentable over Gurunathan et al. (1997) J. Exp. Med., Vol. 186(7), 1137-1147, in view of U.S. Patent No. 6,451,593 (2002), hereafter referred to as Wittig et al., and Makkerh et al. (1996) Current Biology, Vol. 6 (8), 1025-1027, is maintained. Applicant's claim amendments, arguments, and the declaration under

37 CFR 1.132 by the inventors have been fully considered but have not been found persuasive in overcoming the rejection for reasons discussed in detail below.

The applicant argues that the claims are limited to a MIDGE vector encoding p36 LACK antigen covalently linked to an oligopeptide consisting of SEQ ID NO:3. SEQ ID NO:3 is the amino acid sequence PKKKRKV. In their opinion, since Gurunathan et al. teaches a plasmid, not a MIDGE vector, the artisan would not look to this reference. The applicant then argues that Wittig et al. does not disclose PKKKRKV and that Makkerh, while teaching PKKKRKV, doesn't exemplify this embodiment. As such, the applicant argues that impermissible hindsight must have been used to construct the instant rejection.

In response, Gurunathan et al. is clearly analogous art as it teaches a DNA expression construct encoding the p36 LACK antigen from *Leishmania major* operatively linked to the CMV promoter and a polyA sequence and the use of the construct as a vaccine to generate protective immunity against *Leishmania major* in a mammal (Gurunathan et al., pages 1137-1139). The rejection of record further acknowledged that Gurunathan et al. differs from the instant invention in that the DNA expression construct is plasmid not a MIDGE and in that the DNA is not covalently linked to an oligopeptide such as PKKKRKV. However, Wittig et al. was cited to supplement Gurunathan et al. by teaching dumbbell shaped DNA expression constructs comprising covalently closed linear DNA that contains only a coding sequence operably linked to a promoter and polyA termination sequence where the linear ends are linked by short single stranded loops of DNA, and wherein the construct is further covalently linked to a peptide which directs transport of the construct across a cell's endosome or into the nucleus (Wittig et al., claims 1-11, and columns 5-8)). Wittig et al. also teaches a vaccine comprising this construct for

treating infectious diseases (Wittig et al., columns 1 and 8). Wittig et al. was further cited for providing motivation for using a dumbbell DNA expression construct linked to a peptide over a plasmid DNA expression construct. Wittig et al. teaches that because the dumbbell construct consists only of a promoter-gene-terminator sequence, these constructs have none of the disadvantages of plasmid constructs, which include their size, which inhibits fast transport into the cell's nucleus, and the presence of unwanted background sequences, including bacterial sequences, which can lead to unintended immune responses (Wittig et al., columns 2-3, bridging paragraph). Thus, Wittig et al. specifically teaches that the problems with plasmids alluded to by applicants were known in the art and specifically teaches that the use of a dumdbell construct (MIDGE) overcomes these problems. Since Wittig et al. provides clear teachings and motivation to modify the methods of Gurunathan et al., it is not agreed that impermissible hindsight was used to construct the instant rejection.

Turning to the use of an NLS consisting of the sequence PKKKRKV, the rejection stated that Wittig et al. specifically teaches the use of the nuclear localization sequence (NLS) from SV40, a sequence which inherently comprises PKKKRKV (Wittig et al., column 5). While Wittig et al. does not specifically teach that the NLS from SV40 consists of PKKKRKV, at the time of filing, the exact nuclear localization sequence (NLS) of SV40 was known. Makkerh et al. teaches that the sequence consisting of PKKKRKV is the defined nuclear localization sequence of SV40, which can be used to target heterologous molecules to the nucleus (Makkerh et al., page 1025, and Table I, page 1027). As such, the skilled artisan would not only have been motivated to use the PKKKRKV sequence as it is the art recognized NLS of SV40, but would have had a reasonable expectation of success in using PKKRKV as the NLS in a MIDGE-NLS

construct according to Wittig et al. since the substitution of PKKRKV for the NLS comprising PKKRKV disclosed by Wittig et al. represents nothing more than the substitution of one functional equivalent for another with the predictable result of expression of the encoded antigen in the target cell.

The applicant then argues that the declaration by Dr. Marcos Timon-Jimenez under 37 CFR 1.132 demonstrates that the instant claimed invention exhibits unexpected results compared to the prior art constructs. The declaration presents evidence from a post-filing publication by the inventors (Lopez-Fuertes et al. (2002) Vaccine, Vol. 21, 247-257. Unfortunately, while the declaration by Dr. Marcos Timon-Jimenez has been fully and respectfully considered, the declaratory evidence does not establish "unexpected results" in the use of the claimed product such that it is not sufficient to overcome the rejection of record. Specifically, the declaratory evidence is deficient in two aspects. First, the applicant is reminded that any evidence of unexpected results must be commensurate in scope with the claimed invention. MPEP 716.02 (d). In the instant case, the declaration provides the results of experiments which utilize a MIDGE-NLS where the sequence of the NLS is PKKKRKVEDPYC (Lopez-Fuertes et al., page 248, column 2). The instant claims are drawn to an NLS which consists of the sequence PKKKRKV. Thus, the declaratory evidence is not commensurate in scope with the claimed invention. Second, please note that a greater, or greater than additive, effect is not necessarily sufficient to overcome a *prima facie* case of obviousness because such an effect can either be expected or unexpected. *Ex parte The NutraSweet Co.*, 19 USPQ2d 1586 (Bd. Pat. App. & Inter. 1991) and MPEP 716.02 (a). In the instant case, the declaration states that priming and boosting with NLS-modified MIDGE encoding p36 was superior to the best

vaccination protocols available which used priming with plasmid DNA encoding and boosting with rVV. The declaration refers to data set forth in the Lopez-Fuertes et al. post-filing publication of which the inventors were authors. However, while the Lopez-Fuertes et al. publication shows that priming and boosting with MIDGE-p36-NLS results in decreased lesion size compared to priming and boosting with MIDGE-p36 (no NLS), the authors of Lopez-Fuertes et al., including the instant inventors, concluded that prime/boost with MIDGE-p36-NLS induces "at least as good" protection as with prime/boost of plasmid-p36/vaccinia-p36 (Lopez-Fuertes et al., page 252, column 1). In particular, please note that on page 252, column 2, of Lopez-Fuertes et al. it is clearly stated in regards to the results depicted in Table 2 that, "[t]he difference in lesion size between MIDGE-p36-NLS/ MIDGE-p36-NLS and pMOK-p36/rVVp36 immunized animals was not significant". Also on page 252, column 2, the authors state, "[a]s shown in Fig. 2A, the extend of protection triggered by the protocol based on priming/boosting with MIDGE-p36-NLS was similar to that induced by priming/boosting with pMOK-p36 and rVVp36, showing not statistically significant differences between both groups". Thus, the actual results and the clear statements in the Lopez-Fuertes et al. publication that differences seen in Table 2 and Figure 2 between the MIDGE-p36-NLS/ MIDGE-p36-NLS and pMOK-p36/rVVp36 immunized animals were not significantly different do not support applicant's contention of unexpected results. Therefore, since the declaratory evidence is not commensurate in scope with the claimed product and further does not appear to actually demonstrate any "unexpected" results, the declaratory evidence is not found persuasive in overcoming the rejection of record.

***Claim Rejections - 35 USC § 112***

The rejection of claim 24 under 35 U.S.C. 112, second paragraph, for indefiniteness is withdrawn in view of the amendment to claim 24.

The rejection of claim 24 under 35 U.S.C. 112, first paragraph, for new matter is withdrawn in view of the amendment to claim 24.

No claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all

official communications, the new technology center fax number is (571) 273-8300. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

*/Anne Marie S. Wehbé/*
Primary Examiner, A.U. 1633